of fecal fat measurements and calorimetry experiments may not be sufficient to identify small differences between wild-type and knockout animals which over a period of time would be sufficient to explain the observed phenotype. Within these experimental limitations, the data presented herein demonstrate that ERRα mice are lean as a result of aberrant regulation of peripheral lipid mobilization. ERRα mice display an unique combination of properties that suggests that modulation of ERRα activity may provide an effective method to regulate fat metabolism and that ERRα would be a key drug target for the treatment of obesity and other disorders of fat deposition. In addition, the close linkage of ESTRRA and diabetes susceptibility locus IDDM4 (Sladek et al., 1997) together with physiological defects observed in *Estrra*$^{-/-}$ mice suggests that drugs influencing ERRα activity could also be used to treat diabetes and other metabolic disorders.

In the Claims:

Please amend the following claims.

3. (Amended) The non-human transgenic animal of claim 1, wherein said animal is a mammal.

5. (Amended) The non-human transgenic animal of claim 1, displaying a lean phenotype.

6. (Amended) The non-human transgenic animal of claim 1, whose germ cells and somatic cells additionally comprise a transgene encoding a non endogenous ERRα orphan nuclear receptor gene, wherein said transgene is expressed at levels sufficient to complement the disrupted endogenous ERRα orphan nuclear receptor activity.

9. (Amended) A cell line derived from the non-human transgenic animal of claim 1.

15. (Amended) A method for screening and identifying a compound which modulates ERRα orphan nuclear receptor activity, the method including:

a) exposing the non-human transgenic animal of claim 5 to a candidate compound, and;

b) determining the activity of said ERRα orphan nuclear receptor in said animal, wherein an increase in the receptor activity as compared to an unexposed non-human animal is indicative of a compound being capable of increasing ERRα orphan nuclear receptor activity, while a decrease in said receptor activity as compared to an unexposed non-human animal, is indicative of a compound being capable of decreasing ERRα orphan nuclear receptor activity.

18. Method of identifying an agent which modulates fat and/or glucose metabolism *in vivo* comprising:

a) providing a promoter operably linked to a selectable or assayable marker, said promoter being modulated by ERRα;

b) measuring or selecting for said marker in a presence and in an absence of an agent suspected of modulating the promoter modulating activity of ERRα, thereby identifying an agent which modulates ERRα activity wherein a difference in the transcriptional activity in the presence of said agent, as compared to that in the absence thereof, identifies said agent as a modulator of ERRα activity;

c) administering said agent identified in b) to a non-human transgenic animal according to claim 1; and

d) measuring lipid and/or glucose levels in said animal of step c) and comparing same with that of a control animal, not having been administered said agent, wherein a difference in lipid and/or glucose levels of the animal of step c) as compared to that of said control animal identifies said agent as a modulator of fat and/or glucose metabolism *in vivo*.

21. (Amended) The method of claim 20, wherein said mammal is a mouse.

22. (Amended) A modulator of fat and/or glucose metabolism *in vivo* identified by the method of claim 18.

23. (Amended) A method of modulating fat tissue growth and/or weight gain, comprising:

a) administering to an animal an agent which modulates the promoter activity of a gene, wherein said promoter comprises cis-acting elements selected from the group consisting of:

i) an estrogen response element;

ii) TGA AGG TCA;

iii) AGG TCA NNN TGA CCT (SEQ ID NO:1); and

iv) functional variants of i-iii)

such as to modulate the level of said gene, thereby modulating fat tissue growth and/or weight gain in said animal.

28. (Amended) A method of determining whether an agent modulates fat tissue growth and/or weight gain in an animal comprising:

a) providing a transcriptionally active preparation of ERRα or related factors and a DNA sequence comprising a promoter having a cis-acting sequence which modulates activity thereof by an interaction thereto of said ERRα and related factors;

b) measuring said transcriptional activity of said promoter or of a binding of at least ERRα or related factors to said cis-acting sequence in a presence and in an absence of an agent suspected of modulating the transcriptional activity of said promoter or the binding of said factors to said cis-acting sequence, thereby identifying an agent which modulates transcription of said promoter and wherein a difference in the transcriptional activity and/or binding in the presence of said agent, as compared to that in the absence thereof identifies said agent as a modulator of transcription;

c) administering said agent identified in b) to a non-human transgenic animal according to claim 1; and

d) measuring fat tissue growth and/or weight gain in the animal of step c) and comparing same with that of a control animal, not having been administered said agent, wherein a difference in fat tissue growth and/or weight gain of the animal of step c) as compared to that of the control animal identifies said agent as a modulator of fat tissue growth and/or weight gain *in vivo*.

32. (Amended) A modulator of fat and/or glucose metabolism *in vivo* identified by the method of claim 28.

33. (Amended) A method of treating and/or preventing obesity, comprising administering to an obese animal, or an animal susceptible of becoming obese, an agent which modulates the promoter activity of a promoter comprising a cis-acting element selected from the group consisting of:

i) an estrogen response element;

ii) TGA AGG TCA;

iii) AGG TCA NNN TGA CCT (SEQ ID NO:1); and

iv) functional variants of i-iii)

wherein cis-acting element is capable of binding to ERRα.

35. (Amended) A method of determining whether an agent modulates obesity in an animal comprising:

a) providing a transcriptionally active preparation of ERRα or related factors and a DNA sequence comprising a promoter having a cis-acting sequence which modulates activity thereof by an interaction thereto of said ERRα and related factors;

b) measuring said transcriptional activity of said promoter or of a binding of at least ERRα or related factors to said cis-acting sequence in a presence and in an absence of an agent suspected of modulating the transcriptional activity of said promoter or the binding of said factors to said cis-acting sequence, thereby identifying an agent which modulates transcription of said promoter and wherein a difference in the transcriptional activity and/or binding in the presence of said agent, as compared to that in the absence thereof identifies said agent as a modulator of transcription;

c) administering said agent identified in b) to a non-human transgenic animal according to claim 1; and

d) assessing obesity in the animal of step c) and comparing same with that of a control animal, not having been administered said agent, wherein a difference in obesity of the

animal of step c) as compared to that of the control animal identifies said agent as a modulator of obesity *in vivo*.

38. (Amended) The method of claim 37, wherein said mammal is a mouse.

39. (Amended) A modulator of glucose or fat metabolism *in vivo* identified by the method of claim 35.